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Left Ventricular Systolic and Diastolic Function During Acute Coronary Artery Balloon Occlusion in Humans

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Left ventricular function during percutaneous transluminal coronary angioplasty was studied in 16 patients undergoing the procedure. All measurements were performed before and during the first episode of balloon coronary occlusion. In 16 patients (Group A), data were recorded before and 30 or 50 s after balloon inflation, and in 8 of these patients (Group B) data were also recorded 15 min after the complete procedure. Left ventriculograms indicated a marked dyskinesia of the anterior and apical wall in all patients.

After balloon inflation, there was a marked depression in stroke index and ejection fraction and an increase in left ventricular end-diastolic pressure and the time constants of relaxation in all patients. Simultaneous recording of left ventricular pressure (Millar micromanometer) during cineangiography permitted the assessment of myocardial and chamber stiffness. Although there was a strong tendency for both myocardial and chamber stiffness to increase after 30 to 50 s of occlusion, these increases were statistically insignificant.

In Group B, a third set of angiographic and pressure measurements obtained 15 min after completion of the coronary angioplasty procedure indicated no residual left ventricular dysfunction, and in this respect, the results are of added clinical importance.

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The acute changes in left ventricular function after coronary artery ligation have been described in numerous animal studies (1–6). However, it is difficult to extrapolate these results to humans who have different coronary and collateral circulation (7) and in whom atherosclerotic coronary disease may influence the response.

The detection of ischemia-induced wall motion changes in humans has been limited to observations recorded after atrial pacing (8–10) or exercise (11) or during the early stage of acute myocardial infarction (12–14). These studies, however, were conducted 2 to 10 days after the beginning of the symptoms and did not consider the immediate consequences of coronary occlusion.

Percutaneous transluminal coronary angioplasty offers the unique opportunity to study the sequential changes of left ventricular function during the transient occlusion of the vessel. As a consequence, several reports concerning the modifications of myocardial relaxation (15) or coronary blood flow (16,17) during percutaneous transluminal coronary angioplasty have been published. Furthermore, the detection by two-dimensional echocardiography of acute wall motion changes during coronary angioplasty has been described in recent studies (18,19). However, few studies have included the simultaneous recording of left ventricular pressure and left ventricular cineangiograms. Sigwart et al. (20) described the abnormalities of relaxation and segmental wall motion. Serruys et al. (21) reported on the time course of changes during the transient interruption of coronary flow by the balloon occlusion, and Wijns et al. (22) recently described the effect of acute occlusion on left ventricular chamber stiffness.

The aim of this study was to examine the possible changes in left ventricular diastolic and systolic function induced by coronary balloon occlusion in patients with single left anterior descending coronary artery disease, but without angiographic evidence of collateral circulation. If dysfunction occurs, is left ventricular function restored to normal levels after coronary angioplasty?

Methods

Study patients. This study included 16 patients (15 men and 1 woman) who underwent percutaneous transluminal

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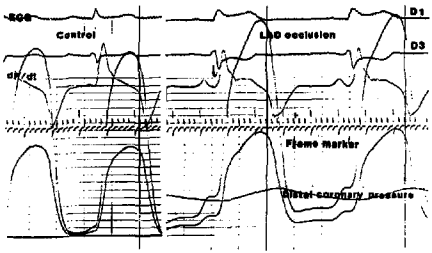

Figure 1. Left ventricular pressure (high and low sensitivity) and the first derivative of pressure (dP/dt) before and during left anterior descending (LAD) coronary artery occlusion. D1 and D3 = electrocardiographic (ECG) leads 1 and 3, respectively.

coronary angioplasty of a proximal left anterior descending coronary artery narrowing. All patients experienced anginal pain on effort and had no history of previous myocardial infarction. All had single significant (>75% luminal diameter reduction) vessel disease and normal left ventricular segmental wall motion. Diagnostic angiography showed no collateral circulation filling the distal left anterior descending coronary artery.

Informed consent was given by all patients. The day before the procedure, they received nifedipine (30 mg) and aspirin (1 g). No drugs except heparin (10,000 IU, intravenously) were given on the day of the procedure.

Study protocol. An 8F pigtail Millar micromanometer was introduced into the left ventricle from the left femoral artery route. The guiding catheter for the angioplasty procedure was introduced from a right femoral artery approach. Left ventricular and aortic pressures were simultaneously recorded. The first left ventricular cineangiogram was performed in the 30° right anterior oblique projection and was obtained by injection of 0.5 ml/kg of sodium and meglumine amidotrizoate. Left ventricular pressures and a frame-marker signal were recorded during cineangiography (Fig. 1). Fifteen minutes later, the narrowing of the left anterior descending coronary artery was crossed and dilated with a 3 mm balloon in 13 patients and with a 3.5 mm balloon in 3 patients. Left ventricular and aortic pressures were recorded, and a second left ventricular cineangiogram was performed during the first coronary balloon inflation. Data were collected at 30 or 50 s after coronary occlusion in 16 patients (Group A). In eight of these patients (Group B), a third ventricular cineangiogram was performed and left ventricular and aortic pressures were recorded 15 min after completion of the procedure. All patients had ST segment elevation during the coronary occlusion and all had successful coronary angioplasty.

Data analysis. Left ventricular and aortic pressures were measured with a computer system (Syscomoran), and frame by frame left ventricular volumes and corresponding pressures were obtained simultaneously from early to end-diastole. Left ventricular contours were detected with the aid of a 6502 microcomputer, and left ventricular volumes were calculated according to the area-length method and the formula of Kennedy et al. (23). Segmental wall motion was measured by the radial method (24), using a center located at 69% of a line joining the upper edge of the aorta to the left ventricular apex in end-systole. Nine radii were obtained in end-diastole and end-systole, and for each, segmental wall shortening was calculated as: segmental wall shortening = 100× (end-diastolic radius − end-systolic radius)/end-diastolic radius. Segments 1, 2, 3 and 4 were related to the anterior wall, segments 6, 7, 8 and 9 corresponded to the inferior wall and segment 5 was related to the apex.

Assessment of chamber and myocardial stiffness constants. Because chamber stiffness (dP/dV) depends on several factors including chamber size (V), myocardial stiffness (E), cavity volume/wall volume ratio (V/Vw) and external constraints, appropriate normalizations must be employed if comparisons between ventricles are to be made.

Specifically, by curve-fitting the diastolic pressure-volume points (P-V) from minimal pressure to end-diastole in the forms:

$$P = A\, e^{\alpha(V/Vw)};\ P = B\, V^{\beta};$$

we obtain

$$dP/(dV/Vw) = \alpha\, A\, e^{\alpha(V/Vw)} = \alpha\, P$$

and

$$dP/(dV/V) = \beta\, B\, V^{\beta} = \beta\, P,$$

where A, B, α and β are curve-fitting variables. Therefore, α (the slope of the dP/[dV/Vw] versus P relation) and β (the slope of the dP/[dV/V] versus P relation) may be employed

Table 1. Hemodynamic Data and Diastolic Function Variables in 16 Group A Patients

	LVEDP (mm Hg)	LVEDVI (ml/m²)	LVESVI (ml/m²)	SVI (ml/m²)	EF (%)	Vw (ml)	Myocardial Stiffness Constants k	δ	β	Chamber Stiffness Constant α	Time Constants of Relaxation (ms) τ_w	τ_m
Pre	20 ± 8	98 ± 17	27 ± 8	70 ±12	72 ± 6	206 ± 44	5.37 ± 1.62	3.23 ± 1.12	1.38 ± 0.43	2.03 ± 0.82	45.6 ± 8.2	47.1 ± 7.9
30,50 s	34 ± 8	104 ± 14	56 ± 14	48 ± 11	46 ± 10		5.62 ± 2.51	4.38 ± 2.33	1.86 ± 0.94	2.42 ± 1.66	60.4 ± 12.5	60.5 ± 12.9
p Value	<0.001	NS	<0.001	<0.001	<0.001		NS	NS	NS	NS	<0.001	<0.005

Data (mean ± SD) are presented in the control state (Pre) and 30 or 50 s after balloon inflation. Four patients were omitted from the paired *t* test analysis for the myocardial and chamber stiffness constants because of nonoverlapping stress and pressure ranges. EF = left ventricular ejection fraction; LVEDP = left ventricular end-diastolic pressure; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; SVI = stroke volume index; Vw = left ventricular wall volume; k, δ and β = myocardial stiffness constants obtained from stress-diameter, pressure-thickness and pressure-volume relations, respectively; α = chamber stiffness constant; τ_w and τ_m = time constants of left ventricular relaxation obtained from two and three constant curve-fits, respectively.

as indexes of chamber and myocardial stiffness, respectively.

Alternative methods (25,26) are presented here for the quantitation of global myocardial stiffness (E) and regional myocardial stiffness (Er) with the results:

$$E = K\,Dm\,(d\,\sigma/d\,Dm) = k\sigma$$

and

$$Er = -\,dP/(dh/h) = \delta\,P,$$

where K is a geometric factor, h is the left ventricular wall thickness, k, β and δ are indexes of myocardial stiffness, Dm is the midwall short-axis diameter and σ is the stress difference. It should be emphasized here that comparisons of chamber stiffness must be made at common levels of pressure and that myocardial stiffness must be compared at common levels of stress.

Assessment of time constants of relaxation. The left ventricular pressure tracings were digitized from the point of peak negative first derivative of left ventricular pressure (dP/dt) to the time at which pressure decreased to 5 mm Hg above end-diastolic pressure. The pressure-time (P-t) data were then curve-fitted in the forms:

$$P = C\,e^{-t/\tau_w};\ P = a + b\,e^{-\gamma t},$$

where τ_w is the time constant as evaluated by the Weiss method (27). The time constant (τ_M) evaluated on the basis of a three constant curve fit (25) is:

$$\tau_M = (1/\gamma)\,\log\,[\,e\,b/(a + b - a\,e)\,].$$

Statistical analysis. All data were expressed as mean ± SD. Paired *t* tests were employed for the 16 patients in Group A who were studied before and after 30 or 50 s of coronary occlusion. An analysis of variance was conducted for the eight Group B patients (restudied 15 min after occlusion) in whom three sequential measurements were made and the statistical significance evaluated by the Bonferroni correction (28).

Results

No complications related to the coronary angioplasty procedure were noted in any of the patients. Tables 1 and 2

Table 2. Hemodynamic Data and Diastolic Function Variables in Eight Group B Patients

	LVEDP (mm Hg)	LVEDVI (ml/m²)	LVESVI (ml/m²)	SVI (ml/m²)	EF (%)	Vw (ml)	Myocardial Stiffness Constants k	δ	β	Chamber Stiffness Constant α	Time Constants of Relaxation (ms) τ_w	τ_m
Pre	22 ± 7	97 ± 14	28 ± 10	68 ± 9	71 ± 8	211 ± 33	4.81 ± 1.64	3.12 ± 1.10	1.32 ± 0.48	1.99 ± 0.71	43.4 ± 5.4	46.1 ± 7.5
50 s	34 ± 8	105 ± 16	57 ± 18	48 ± 9	46 ± 10		4.82 ± 1.53	3.47 ± 1.23	1.48 ± 0.47	1.97 ± 0.71	57.7 ± 10.5	59.2 ± 13.2
Post	21 ± 6	99 ± 17	28 ± 16	72 ± 13	72 ± 12		4.56 ± 1.52	3.53 ± 1.95	1.64 ± 0.90	2.13 ± 1.03	42.5 ± 6.4	43.8 ± 7.3
p Value (Pre vs. 50 s)	<0.01	NS	<0.005	<0.005	<0.005		NS	NS	NS	NS	<0.005	<0.03

Data (mean ± SD) are presented in the control state (Pre), 50 s after balloon inflation (50 s) and 15 min after the complete procedure (Post). Probability (p) values based on an analysis of variance refer to the 50 s state relative to the control state (Pre). All hemodynamic and diastolic function variables returned to near control levels 15 min after the complete procedure. Abbreviations as in Table 1.

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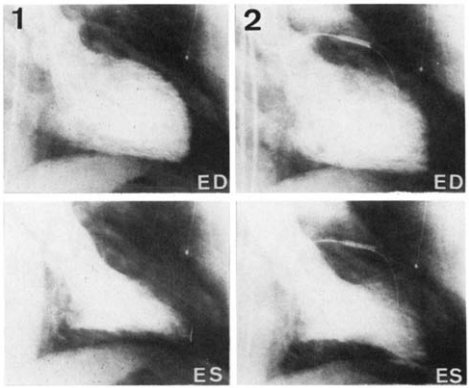


Figure 2. Left ventricular cineangiograms before and during coronary occlusion in end-diastole (ED) (**upper panel**) and end-systole (ES) (**lower panel**).

summarize the data for both groups of patients.

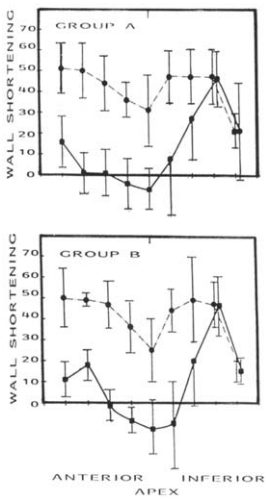
Left ventricular pressures. Left ventricular end-diastolic pressures (Tables 1 and 2) were significantly increased ($p < 0.01$) at 30 or 50 s of occlusion and the magnitudes of these increases were similar in both groups.

Segmental wall motion. The visual analysis of the left ventricular cineangiogram during coronary occlusion clearly demonstrated a marked dyskinesia of the anterior and apical walls in all patients. Figures 2 and 3 show the important modifications that occurred during total occlusion of the left anterior descending coronary artery: occlusion for 30 or 50 s resulted in a marked decrease in the anterior and antero-apical wall shortening fraction with the appearance of a systolic outward displacement.

Left ventricular volumes and ejection fraction. Complete occlusion of the left anterior descending coronary artery resulted in a significant increase ($p < 0.001$) in left ventricular end-systolic volume index from 27 ± 8 to 56 ± 14 ml/m^2 in Group A (Table 1) and from 28 ± 10 to 57 ± 18 ml/m^2 in Group B ($p < 0.005$) (Table 2). Left ventricular end-diastolic volume index was slightly (but insignificantly) increased at 30 or 50 s of occlusion, and a dramatic and significant decrease in stroke index and ejection fraction was noted ($p < 0.005$). Thus, occlusion of the left anterior descending coronary artery for 30 or 50 s resulted in a marked depression of left ventricular systolic function.

Time constants of relaxation (τ_w, τ_M) (Tables 1 and 2). Occlusion of the left anterior descending coronary artery for 30 or 50 s in Group A patients resulted in important and significant increases in τ_w from 46 ± 8 to 60 ± 12 ms ($p <$

Figure 3. Wall shortening (%) 30 s after balloon inflation (**upper panel**) and after 50 s inflation (**lower panel**). **Dashed lines** = before coronary occlusion; **continuous lines** = during coronary occlusion.



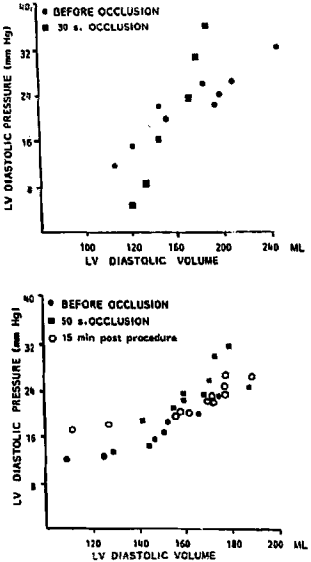


Figure 4. Left ventricular (LV) diastolic pressure-volume relations in a typical patient from each group. **Upper panel.** Pressure-volume relation in a Group A patient before (●) and after 30 s (■) of occlusion. **Lower panel.** Pressure-volume relation in a Group B patient before (●) occlusion, at 50 s of occlusion (■) and 15 min after completion of the angioplasty procedure (○). Note the upward shifts in these relations after coronary occlusion. In Group B, the pressure-volume relations return to preocclusion levels 15 min after the procedure.

0.001) and in τ_M from 47 ± 8 to 60 ± 13 ms ($p < 0.005$). Significant increases were also observed in patients in Group B. The time constant τ_w increased from 43 ± 5 to 58 ± 10 ms ($p < 0.005$) and τ_M increased from 46 ± 8 to 59 ± 13 ms ($p < 0.03$). In patients in Group B, both time constants returned to preocclusion levels 15 min after the procedure.

Chamber stiffness constant (α). Because chamber stiffness must be compared at common levels of pressure, four patients were excluded from the statistical analysis. No significant alterations were observed in the chamber stiffness constant (α) after coronary occlusion at 30 or 50 s (Groups A and B) or at 15 min (Group B). In Group A, α increased from 2.03 ± 0.82 to 2.42 ± 1.66, and in Group B, α was unaltered (pre: 1.99 ± 0.71; 50 s: 1.97 ± 0.71). Fifteen minutes after the procedure in the Group B patients, α remained within the preocclusion levels (2.13 ± 1.03) (Fig. 4).

Table 3. Values of Myocardial Stiffness Constants for Groups A and B

	k	δ	β
Group A			
Pre	5.37 ± 1.62	3.23 ± 1.12	1.38 ± 0.43
30-50 s	5.62 ± 2.51	4.38 ± 2.33	1.86 ± 0.94
Group B			
Pre	4.81 ± 1.64	3.12 ± 1.10	1.32 ± 0.48
50 s	4.82 ± 1.53	3.47 ± 1.23	1.48 ± 0.47
15 min	4.56 ± 1.52	3.53 ± 1.95	1.64 ± 0.90

Pre = preocclusion.

Myocardial stiffness constants (k, β and δ). The myocardial stiffness constants were evaluated by three different methods, and each yielded the same qualitative results for each group. Although there was generally a tendency for myocardial stiffness to increase after coronary occlusion for 30 or 50 s, these alterations were not statistically significant. In Group B, preocclusion levels were maintained 15 min after the procedure. The values for these constants are shown in Table 3.

Discussion

Left ventricular abnormalities due to ischemia. Left ventricular systolic and diastolic function are markedly affected shortly after occlusion of the left anterior descending coronary artery. Stroke volume and ejection fraction decreased, left ventricular end-diastolic pressure increased and left ventricular relaxation was prolonged. There was a tendency for both chamber and myocardial stiffness to increase, indicating a reduction in left ventricular compliance; however, these changes were not statistically significant. Generally, these results were similar to those in previous animal studies (1–4); however, in coronary artery occlusion experiments, the pressure-segment length relation has repeatedly been shown to move to the right. The present study involved patients with single vessel coronary artery disease and significant narrowing of the proximal left anterior descending coronary artery. Thus, interruption of coronary flow induced by transient balloon inflation during percutaneous transluminal coronary angioplasty is a situation that completely mimics the experimental coronary artery ligation performed during animal studies.

The results of the present study agree, in part, qualitatively with those previously described (21,22), namely, 1) there were upward shifts in the diastolic pressure-volume relations immediately after the angioplasty procedure, and 2) systolic function and the time constants of relaxation re-

turned to near preocclusion levels 12 to 15 min after completion of the procedure. In contrast, these studies showed that abnormalities in the chamber stiffness persisted 12 min after the procedure, a result not observed in the present study.

There may be several reasons for this disagreement. In the previous studies (22), pressure and angiographic measurements were obtained 20 s during the second dilation and 50 s during the fourth dilation. The interval between two sequential angiograms was at least 10 min, and one cannot exclude the possible influence of contrast medium in these consecutive examinations. Moreover, immediate collateral circulation may occur after a first coronary artery occlusion. In the present study, all measurements at 30 and 50 s were done during the first balloon inflation.

Another possible explanation for these differences may reside in the different methods employed for the assessment of chamber stiffness. Global stiffness, and not regional chamber stiffness, was analyzed in this study. However, the earlier studies (22) considered variables of chamber stiffness that were size dependent, and comparisons were not always conducted over common pressure ranges.

Relation between ventricular asynergy and diastolic function. After 30 or 50 s of coronary artery occlusion, left ventricular systolic function is dramatically depressed with a marked decrease of the ejection fraction because of an increase in end-systolic volume. This is clearly related to the large ischemic area as demonstrated by the depression of wall motion shortening, which specifically affected the anterior and apical segments. In both groups, a systolic outward displacement of the ischemic segment was observed. Serruys et al. (21) showed that the moment of maximal wall displacement for the anterior wall shifted from end-systole to early diastole. This late systolic outward displacement of the ischemic segment is probably passive and could be due to the increased inward displacement of the nonischemic segments. This is similar to the results obtained by Tyberg et al. (30), who described the relation between transient asynergy, myocardial ischemia and alteration in the time course of relaxation, and observed that the prolongation of this variable was seen only on reoxygenation. In human patients, the prolongation of time constant of the early relaxation phase is the earliest hemodynamic marker of myocardial ischemia. In both our groups of patients, marked increases were observed in the time constants of relaxation (τ_w, τ_M). By a careful analysis of the left ventricular cineangiogram, Serruys et al. (21) showed that these changes accompanied a biphasic wall displacement of the ischemic area after aortic valve closure. The deformation occurring in the ascending limb of the negative dP/dt tracing (Fig. 1) occurred simultaneously with the beginning of the second wave of inward displacement. It should be noted that after 50 s of occlusion, the time constant is not significantly different from the preocclusion values, and generally the deformation of peak negative dP/dt disappeared.

Indexes of chamber and myocardial stiffness. Indexes of chamber and myocardial stiffness employed in this study are dimensionless and, therefore, are more appropriate for comparison purposes. This has generally not been the case in most previous studies relating to the assessment of chamber stiffness in particular. This fact, in addition to the dependence of chamber stiffness on a number of important factors (25,29), is the main reason for the difficulty in developing useful and sensitive indexes of chamber and wall stiffness that can be applied in the clinical setting.

Although three approaches were employed here for the assessment of myocardial stiffness, these indexes also have their limitations. The stiffness constants k and β describe global stiffness, and may not be valid in cases of segmental disease as considered in the present study. On the other hand, the radial stiffness constant δ does more closely represent a regional stiffness variable. However, the possibility exists that pericardial pressure may have been elevated during these procedures and was not accounted for in these or the earlier studies (21,22). Thus, future studies should include measurements of right atrial pressures (31), enabling one to consider, in a semiquantitative manner, these pericardial effects.

Clinical implications. The results of the present studies and those of others (21,22) have important clinical implications since changes in left ventricular systolic and diastolic function were observed as early as 30 or 50 s after coronary artery occlusion. Generally, diastolic variables returned to preocclusion values; however, there may be a subset of patients in whom dysfunction persists after completion of the coronary angioplasty procedure. Many more studies need to be conducted and more sophisticated methods for analyzing chamber and myocardial stiffness need to be developed along the lines described by Pasipoularides et al. (32).

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